More Than Meets the Skin: Disseminated Histoplasmosis Hidden Behind HSV

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Abstract

- This case involves a 67-year-old male with follicular lymphoma undergoing active immunotherapy with Glofitamab/Obinutuzumab, who presented with altered mental status and a diffuse rash. He was transferred to our facility for nephrology evaluation. Treatment for suspected VZV was initiated, however his rash continued to progress. Multiple skin biopsies had been completed, all confirming VZV only. Infectious workup was broadened and revealed positive urinary histoplasma antigen and amphotericin was initiated. This suggested possible coinfection with both histoplasma and VZV. He continued to clinically decompensate despite both therapies.

Introduction

- A 67-year-old male with follicular lymphoma presented with altered mental status and a diffuse rash. He was immunocompromised secondary to active immunotherapy with glofitamab/obinutuzumab. He had been recently diagnosed with disseminated varicella zoster virus (VZV) and treated with IV acyclovir, but did not complete therapy due to gastrointestinal side effects. His medical history includes cirrhosis due to metabolic dysfunction-associated steatohepatitis (MASH), coronary artery disease, chronic kidney disease (CKD) stage IV, type 2 diabetes mellitus.
- Glofitamab belongs to a class of bispecific T-cell engager (BiTE) antibody, that is typically utilized to treat refractory B-cell Lymphoma, typically diffuse large B-Cell Lymphoma. BiTE therapies, including glofitamab, are associated with profound immunosuppression and increased risk for opportunistic infections.[1] Reactivation of VZV and invasive fungal infections, such as histoplasmosis, are well-documented in this population.[2,3] Co-infection with both pathogens is exceedingly rare and there is limited data regarding infectious complications specific to bispecific antibody regimens.

Methodology

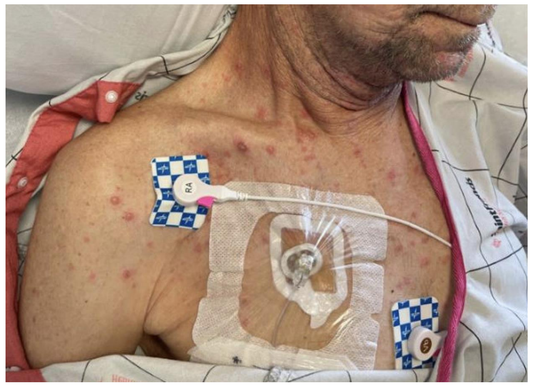

Figure 1: Rash presentation on 07/24 with initial diagnosis of Herpes Zoster

- On physical exam, a non-specific diffuse vesicular rash was localized to his face, trunk, extremities, and palms/soles. The initial rash is pictured above (figure 1) during initial presentation on 07/24 to outlying facility, a few weeks prior. Figure 2 below shows the progression of the rash dated 08/08 upon presentation during the discussed hospitalization.

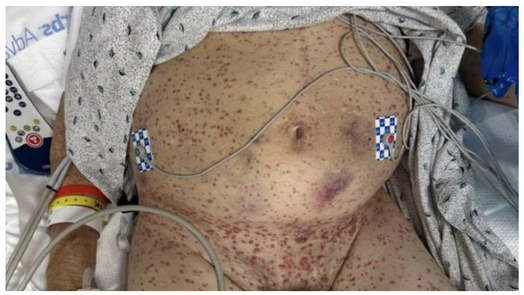

Figure 2: Rash presentation on 08/08 following multiple doses of acyclovir at OLF

Results

- On arrival, he was re-initiated on intravenous acyclovir given his previous diagnosis of VZV and incomplete prior treatment. He was prescribed a 21 day course of oral acyclovir on prior discharge, but only completed ”a few days”.
- Multiple sub-specialists were consulted on this case including Dermatology, Infectious Disease, Nephrology and Oncology. Many alternative diagnoses were considered such as Sweet syndrome, Histoplasmosis, Syphilis, ITP, AIN. The lesions continued to progress despite Acyclovir, and concern remained for possibly Acyclovir resistance. His mentation remained persistently AOx1.
- A urinary histoplasma antigen was positive (1.13 ng/mL), and Amphotericin B was initiated on 08/15. We additionally tested IgG levels which were low, and the patient received a one-time dose of IVIG. His platelets decreased from 204 on arrival to as low as 18. His GFR remained 20 (baseline 35) for the duration of his hospitalization.
- Despite maximal supportive care, his condition deteriorated resulting in multi-system organ failure requiring intubation. He subsequently developed new onset atrial fibrillation with RVR. His condition did not improve resulting in his death on 08/18. Postmortem skin biopsy confirmed VZV but remained negative for histoplasma, consistent with prior biopsy results.

Conclusion

- This is one of the first documented cases of co-infection by VZV and histoplasmosis with a patient actively undergoing glofitamab therapy. The patient’s initial cutaneous eruption was attributed to VZV, delaying recognition of fungal co-infection. The continued absence of histoplasma on skin biopsy despite urinary antigen positivity is unique, and underscores diagnostic limitations of localized testing in systemic disease. Clinicians should maintain a high index of suspicion for multiple co-exisiting opportunistic infections, as early broad infectious workups can prevent diagnostic delays. Recognition of emerging infectious risks associated with novel immunotherapies is essential to improving outcomes in this vulnerable population.

References

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